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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KALLIS, RUSSELL	
ART UNIT	**PAPER NUMBER**
1638	

DATE MAILED: 01/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

SM.

Office Action Summary	Application No.	Applicant(s)	
	09/026,400	MORI ET AL.	
	Examiner	Art Unit	
	Russell Kallis	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-11 and 13-24* is/are pending in the application.

4a) Of the above claim(s) *14-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-11,13 and 21-24* is/are rejected.

7)☒ Claim(s) *8* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/14/2003 has been entered.

Claims 2-11, 13-21 and newly added Claims 22-24 are pending and Claims 2-11, 13, 21-24 are examined.

Claim Objections

Claim 8 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

A series of singular dependent claims is permissible in which a dependent claim refers to a preceding claim which, in turn, refers to another preceding claim.

A claim which depends from a dependent claim should not be separated by any claim which does not also depend from said dependent claim. It should be kept in mind that a dependent claim may refer to any preceding independent claim. In general, applicant's sequence will not be changed. See MPEP § 608.01(n).

Further, Claim 8 should follow Claim 23.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2, 5-11, and 21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant broadly claims any isolated nucleic acid that hybridizes, under conditions of moderate stringency, to degenerate sequences that encodes an amino acid sequence of SEQ ID NO: 2 or 4, amplified by PCR with primers of SEQ ID NO: 5 or 6 (degenerate 5' oligo primers made from the N-terminal of a barley nicotianamine aminotrasferase enzyme) and the encoded amino acid sequence having nicotianamine aminotransferase activity. It is noted that the claims are not drawn to sequences which hybridize to the DNA sequences of SEQ ID NO: 1 or 3 and that have nicotianamine aminotransferase activity.

Applicant describes barley cDNA of SEQ ID NO: 1 and 3 encoding SEQ ID NO: 2 and 4.

Applicant does not describe any isolated cDNA encoding a protein that has nicotianamine aminotransferase activity, other than SEQ ID NO: 1 and 3 encoding SEQ ID NO: 2 and 4; or any conserved sequences of SEQ ID NO: 2 and 4 that could be correlated with any other proteins having nicotianamine aminotransferase activity.

Given the claim breadth and lack of guidance as discussed above, the specification does not provide an adequate written description of the claimed invention.

See *University of California V. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism.

The court also addressed the manner by which genus of cDNAs might be described: "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." *Id.* At 1406.

Based upon the disclosure of SEQ ID NO: 1 and 3, there is insufficient relevant identifying characteristics to allow one skilled in the art to completely determine the structure of nucleic acids that hybridize to a nucleotide sequence encoding SEQ ID NO: 2 or 4, amplifiable by PCR from isolated nucleic acids of the Gramineae using SEQ ID NO: 5 and 6, and have nicotianamine aminotransferase activity including mutants and allelic variants, absent further guidance. Since the claimed genus encompasses undisclosed or yet to be discovered sequences that amplify by PCR with primers of SEQ ID NO: 5 or 6 (degenerate oligo primers made from the N-terminal of a barley nicotianamine aminotrasferase enzyme) and hybridize to a nucleotide sequence that encodes either SEQ ID NO: 2 or 4 and encode an amino acid sequence having nicotianamine aminotransferase activity, the disclosure of SEQ ID NO: 1 and 3 encoding SEQ

ID NO: 3 and 4 does not provide adequate description of the claimed genus. In view of the level of knowledge and skill in the art one skilled in the art would not recognize from Applicant's disclosure that Applicant was in possession of the nucleic acids that hybridize to SEQ ID NO: 1 or 3, amplified by PCR from isolated nucleic acids of the Gramineae using SEQ ID NO: 5 or 6, and that have nicotianamine aminotransferase activity, as broadly claimed.

Given the failure of the broadly claimed genus encompasses undisclosed or yet to be discovered sequences that hybridize to a nucleotide sequence encoding SEQ ID NO: 2 or 4, that are amplifiable using SEQ ID NO: 5 and 6, and that have nicotianamine aminotransferase activity to be adequately described, methods of its use are also inadequately described. See Written Description Guidelines, Federal Register Vol. 66 No. 4, Friday January 5, 2001 "Notices", pages 1099-1111.

Applicant asserts that the Mehta P.K. et al. (Eur. J. Biochem. 1989, Vol. 186, pages 249-253) reference teaches sufficient structural information about the claimed genus of nucleic acids from Gramineae in the form of conserved amino acid residues of aminotransferases that are also conserved in SEQ ID NO: 2, such that when combined with the limitations of having nicotianamine aminotransferase activity and hybridization to a nucleotide sequence amplified from Gramineae by SEQ ID NO: 5 or 6 and that encodes SEQ ID NO: 2 or 4 is sufficient written description (response pages 13-15). The conserved sequences suggested by applicant partially define aminotransferases in general, but do not provide for a written description of the genus of nicotianamine aminotransferases from the 9,000 Gramineae species that comprise 20% of the earth's vegetation.

Claims 2, 5-11, and 21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated DNA encoding a nicotianamine aminotrasferase of SEQ ID NO: 2 or 4, vectors, transformed plant and bacterial cells, and transgenic plants comprising said DNA, as well as a method of enhancing iron absorbing of a plant with said DNA when grown in alkaline soils, does not reasonably provide enablement for any isolated nucleic acid from the Gramineae that amplifies by PCR with primers of SEQ ID NO: 5 or 6 (degenerate 5' oligo primers made from the N-terminal of a barley nicotianamine aminotrasferase enzyme) and hybridizes to a nucleotide sequence that encodes either SEQ ID NO: 2 or 4 and encodes an amino acid sequence having nicotianamine aminotransferase activity and a method of enhancing iron absorbing of a plant with said DNA when grown at any soil pH. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Applicant broadly claims any isolated nucleic acid that hybridizes, under conditions of moderate stringency, to degenerate sequences that encodes an amino acid sequence of SEQ ID NO: 2 or 4, amplified by PCR with primers of SEQ ID NO: 5 or 6 (degenerate 5' oligo primers made from the N-terminal of a barley nicotianamine aminotrasferase enzyme) and the encoded amino acid sequence having nicotianamine aminotransferase activity. It is noted that the claims are not drawn to sequences which hybridize to the DNA sequences of SEQ ID NO: 1 or 3 and that have nicotianamine aminotransferase activity.

Applicant teaches PCR amplification of a cDNA from isolated barley mRNA, enriched for iron deficiency expression, using degenerate oligo primers of SEQ ID NO: 5 and 6 made from the N terminal of an isolated barley nicotianamine aminotrasferase enzyme; the use of the

amplified cDNA as a probe, under moderate hybridization conditions, to isolated barley cDNA of SEQ ID NO: 1 and 3 encoding SEQ ID NO: 2 and 4 (examples 1-5); and a method of determining nicotianamine aminotransferase activity (page 7 of specification).

Applicant does not teach any isolated cDNA encoding a protein that has nicotianamine aminotransferase activity, other than SEQ ID NO: 1 and 3 encoding SEQ ID NO: 2 and 4; or the amplification of any other nicotianamine aminotrasferase encoding cDNA using SEQ ID NO: 5 and 6 that hybridizes to a nucleotide sequence encoding SEQ ID NO: 2 or 4 from any other Gramineae plant other than barley.

The unpredictability in isolating a cDNA that encodes an enzyme having nicotianamine aminotransferase activity from any one of the multitude of plant species or varieties of Gramineae using degenerate primers derived from a non-conserved region of a single barley nicotianamine aminotransferase coding sequence is quite significant when considering the sequence variation that is inherent in Gramineae plants of global geographical distribution comprising 9,000 species and 20% of the earth's vegetation, variation in ploidy levels, and allelic variation; and when also considering that the degenerate 5' primers would amplify sequences other than those encoding a cDNA having nicotianamine aminotransferase activity, whether the mRNA pool is enriched or not, and that the moderate to low stringency of the hybridization and wash conditions of the claimed method would yield sequences other than those claimed.

Given the unpredictability in the art as to which Gramineae species would recover an amplified PCR product having nicotianamine aminotransferase activity using degenerate primers of SEQ ID NO: 5 or 6 from barley; the breadth of the claims encompassing any isolated nucleic acid that hybridizes, under conditions of moderate stringency, to a nucleotide sequence that

encodes either SEQ ID NO: 2 or 4, amplified by PCR with primers of SEQ ID NO: 5 or 6 and encodes an amino acid sequence having nicotianamine aminotransferase activity; the lack of guidance in the examples of the specification or in the prior art as to which members of the Gramineae would yield a nicotianimine aminotransferase cDNA by PCR using SEQ ID NO: 5 or 6; although one of skill in the art can readily isolate mRNA and amplify a cDNA sequence, one would not know based upon Applicant's disclosure which embodiments would be inoperable and predictable eliminated, and thus undue trial and error experimentation would be needed by one skilled in the art to make and clone a multitude of non-exemplified variants of PCR reaction products that hybridize to a nucleotide sequence that encodes SEQ ID NO: 2 and 4, and would require one of skill in the art to test a myriad of PCR amplified sequences for nicotianimine transferase activity. Therefore, the invention is not enabled for the scope set forth in the claims.

Applicant asserts that the specification in combination with the teachings of the Mehta P.K. et al. reference (Eur. J. Biochem. 1989, Vol. 186, pages 249-253) is enabling for isolating a nicotianamine aminotrasferase from any one of the species of Gramineae (response page 15-17).

The response to Applicant's enablement traversal is addressed in the enablement rejection supra.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 2-11, 13, and 21-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

At Claim 2, 5, 6, 7, 11, and 21, wherein the claim recites "a nucleotide sequence of DNA which is amplifiable by polymerase chain reaction on a nucleic acid from a Gramineae plant" is indefinite because the PCR reaction conditions are not described and thus the amplified DNA could be any Gramineae DNA.

At Claim 7, for clarity insert in part (3) after "cell," --wherein the promoter, the nucleotide sequence, and the terminator are--. While the preamble recites "expression plasmid", none of the components are placed in an expression plasmid.

At Claim 8 "as defined in Claim 5, 6, 22, or 23" is indefinite. It is not clear if more than one claim is defining the plasmid. Further, dependent claims follow the claims from which they depend. Furthermore, multiple dependent claims should be recited in the alternative e.g. "any one of claims 1, 2, or 3".

At Claim 11 the method claim is indefinite because it fails to recite all the method steps that show the claim of a process for enhancing iron absorption in a plant is complete. The claim language "which absorbs iron" suggests that the plant cell is already capable of absorbing iron prior to transformation. Further, the claim also does not clearly recite the method steps in the order in which they must occur, namely that the plant is transformed, the nucleotide sequence encoding the nicotianamine aminotransferase is transcribed, the expressed protein catalyzes the formation of a mugeneic acid compound that solubilizes iron, and wherein the ability of the plant to absorb iron is enhanced when grown in alkaline soil. Appropriate action is required.

At Claim 13 "the nucleic acid" lacks antecedence.

Claims 2-11, 13, and 21-24 are deemed free of the prior art, given the failure of the prior art to teach or reasonably suggest a nucleotide sequence encoding an amino acid sequence of SEQ ID NO: 2 or 4 having nicotianamine aminotransferase activity, or a method for enhancing iron production in a plant therewith.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (703) 305-5417. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0198.

Russell Kallis Ph.D.
November 21, 2003

PHUONG T. BUI
PRIMARY EXAMINER
12/1/03